Inside This Issue of JACC

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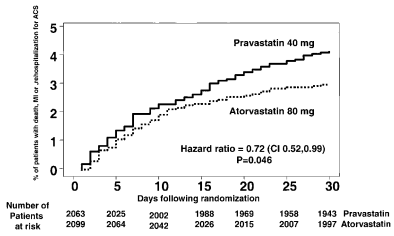

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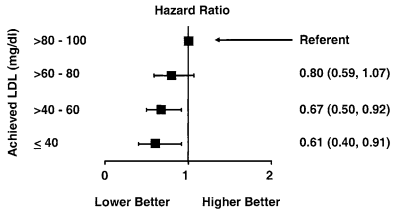

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Focus Issue: PROVE IT-TIMI 22

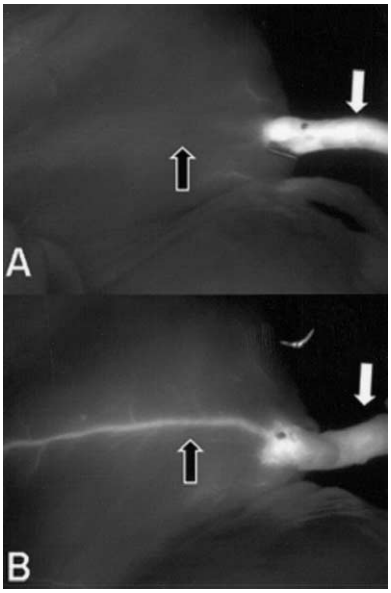
Implications of the PROVE IT-TIMI 22 Trial

The PROVE IT-TIMI 22 trial randomized over 4,000 subjects with acute coronary syndromes (ACS) to either moderate (average low-density lipoprotein [LDL] 62 mg/dl) or intensive (average LDL 95 mg/dl) lipid lowering. Intensive therapy was superior to moderate with a 16% reduction in the primary endpoint. This trial provides strong support for the "lower is better" theory of lipid modification; the robust dataset enable the four papers in this focus issue to examine why. Ray and colleagues examined the timing of the benefit seen in PROVE IT-TIMI 22 trial. They found a relative risk reduction of nearly 30% in both the first 30 days and 6 months after an ACS, suggesting that intensive statin therapy provides "two windows of cardioprotection" and should begin in-hospital and continue for the long term. Wiviott and colleagues examined the safety of extremely low LDL by determining the rates of adverse events stratified by LDL levels, including the 10% of subjects who had LDLs <40 mg/dl. No relationship was found between achieved LDL level and either statin side effects or adverse events postulated to be secondary to low cholesterol. The benefits, however, continued to improve with these very low LDL levels. Another paper by Ray and colleagues focuses on the relationship between C-reactive protein (CRP) and intensive lipid lowering. Several metabolic and lifestyle risk factors were associated with higher CRP levels, such that CRP was found to be a "global barometer" of cardiovascular risk. In a final paper, Ray and Cannon discuss the evidence that statins exert a beneficial effect that is disproportionate to the LDL reduction: supporting the benefits of pleiotropic effects. **See pages 1405, 1411, 1417, and 1425. See figures.**

Simon Dack Lecture

Identifying Genetic Risk Factors for Myocardial Infarction

At the 2005 ACC conference, Dr. Eric Topol delivered the keynote Simon Dack Lecture. This reprint of his address explores the past, present, and future of the ability of genomic techniques to identify heritable factors that predispose to myocardial infarctions. The speech can serve as a primer to the techniques used to identify suspected genes as it guides us through the recent breakthroughs in genotyping technology. He touches on several emerging sequencing techniques along with the development of a core map of the genome that should speed the discovery process over the next decade. He expresses hope that we are on the precipice of understanding these genetic risk factors and eventually to individually tailored therapies. **See page 1456.**



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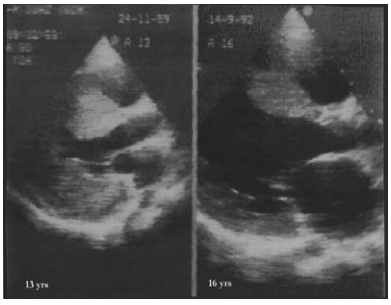
Cardiac Surgery

Intraoperative Assessment of Coronary Bypass Grafts

A certain percentage of coronary artery bypass grafts occlude shortly after surgery. While neither the frequency nor the etiology is known, visualizing graft patency intraoperatively might allow problems to be identified early and repaired. Desai and colleagues describe a technique using fluorescent indocyanine green (ICG) dye to visualize the recently implanted grafts and the native coronary vessels. ICG is thought to be non-toxic; when excited with a laser light it emits a characteristic frequency of light that can be visualized using a CCD. In 120 patients undergoing bypass surgery, problems with a graft that required revision were found in 4% of patients despite apparent success to the surgeons. This technique may allow for real time visualization of bypass grafts and improvements in graft patency before leaving the operating room. **See page 1521. See figure.**



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Hypertrophic Cardiomyopathy

Frequency of Transition From Hypertrophic to Dilated Cardiomyopathy

That a certain percentage of patients with hypertrophic cardiomyopathy (HCM) will transition to a hypokinetic dilated cardiomyopathy (DCM) is known, but poorly understood. Biagini and colleagues report that in a large cohort of HCM patients followed for a mean of 12 years, the incidence of the transition is 5.3 per 1,000 patient-years. Those who had transitioned to DCM were younger and more likely to have a family history of HCM, and more pronounced hypertrophy. Clinically, they were more likely to die or require heart transplantation. Further understanding the transition from HCM to DCM has important clinical and biologic ramifications. **See page 1543. See figure.**